



980232_1.TXT

SEQUENCE LISTING

<110> NICOLAIDES, NICHOLAS
VOGELSTEIN, BERT
KINZLER, KINZLER

<120> A METHOD FOR GENERATING HYPERMUTABLE
ORGANISMS

<130> 01107.00004

<140> 09/558149

<141> 2000-04-26

<150> 09/059461

<151> 1998-04-14

<160> 8

<170> FastSEQ for Windows Version 4.0

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<212> DNA

<213> Homo sapiens

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Glu Pro Ala Lys Ala Ile Lys Pro Ile Asp Arg Lys Ser Val His Gln
10 15 20 25

att tgc tct ggg cag gtg gta ctg agt cta agc act gcg gta aag gag 147
Ile Cys Ser Gly Gln Val Val Leu Ser Leu Ser Thr Ala Val Lys Glu
30 35 40

tta gta gaa aac agt ctg gat gct ggt gcc act aat att gat cta aag 195
Leu Val Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn Ile Asp Leu Lys
45 50 55

ctt aag gac tat gga gtg gat ctt att gaa gtt tca gac aat gga tgt 243
Leu Lys Asp Tyr Gly Val Asp Leu Ile Glu Val Ser Asp Asn Gly Cys
60 65 70

ggg gta gaa gaa gaa aac ttc gaa ggc tta act ctg aaa cat cac aca 291
Gly Val Glu Glu Glu Asn Phe Glu Gly Leu Thr Leu Lys His His Thr
75 80 85

tct aag att caa gag ttt gcc gac cta act cag gtt gaa act ttt ggc 339
Ser Lys Ile Gln Glu Phe Ala Asp Leu Thr Gln Val Glu Thr Phe Gly
90 95 100 105

980232_1.TXT

ttt cgg ggg gaa gct ctg agc tca ctt tgt gca ctg agc gat gtc acc	387
Phe Arg Gly Glu Ala Leu Ser Ser Leu Cys Ala Leu Ser Asp Val Thr	
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att tct acc tgc cac gca tcg gcg aag gtt gga act cga ctg atg ttt	435
Ile Ser Thr Cys His Ala Ser Ala Lys Val Gly Thr Arg Leu Met Phe	
125 130 135	
gat cac aat ggg aaa att atc cag aaa acc ccc tac ccc cgc ccc aga	483
Asp His Asn Gly Lys Ile Ile Gln Lys Thr Pro Tyr Pro Arg Pro Arg	
140 145 150	
ggg acc aca gtc agc gtg cag cag tta ttt tcc aca cta cct gtg cgc	531
Gly Thr Thr Val Ser Val Gln Gln Leu Phe Ser Thr Leu Pro Val Arg	
155 160 165	
cat aag gaa ttt caa agg aat att aag aag gag tat gcc aaa atg gtc	579
His Lys Glu Phe Gln Arg Asn Ile Lys Lys Glu Tyr Ala Lys Met Val	
170 175 180 185	
cag gtc tta cat gca tac tgt atc att tca gca ggc atc cgt gta agt	627
Gln Val Leu His Ala Tyr Cys Ile Ile Ser Ala Gly Ile Arg Val Ser	
190 195 200	
tgc acc aat cag ctt gga caa gga aaa cga cag cct gtg gta tgc aca	675
Cys Thr Asn Gln Leu Gly Gln Gly Lys Arg Gln Pro Val Val Cys Thr	
205 210 215	
ggg gga agc ccc agc ata aag gaa aat atc ggc tct gtg ttt ggg cag	723
Gly Gly Ser Pro Ser Ile Lys Glu Asn Ile Gly Ser Val Phe Gly Gln	
220 225 230	
aag cag ttg caa agc ctc att cct ttt gtt cag ctg ccc cct agt gac	771
Lys Gln Leu Gln Ser Leu Ile Pro Phe Val Gln Leu Pro Pro Ser Asp	
235 240 245	
tcc gtg tgt gaa gag tac ggt ttg agc tgt tcg gat gct ctg cat aat	819
Ser Val Cys Glu Glu Tyr Gly Leu Ser Cys Ser Asp Ala Leu His Asn	
250 255 260 265	
ctt ttt tac atc tca ggt ttc att tca caa tgc acg cat gga gtt gga	867
Leu Phe Tyr Ile Ser Gly Phe Ile Ser Gln Cys Thr His Gly Val Gly	
270 275 280	
agg agt tca aca gac aga cag ttt ttc ttt atc aac cgg cgg cct tgt	915
Arg Ser Ser Thr Asp Arg Gln Phe Phe Phe Ile Asn Arg Arg Pro Cys	
285 290 295	
gac cca gca aag gtc tgc aga ctc gtg aat gag gtc tac cac atg tat	963
Asp Pro Ala Lys Val Cys Arg Leu Val Asn Glu Val Tyr His Met Tyr	
300 305 310	
aat cga cac cag tat cca ttt gtt gtt ctt aac att tct gtt gat tca	1011
Asn Arg His Gln Tyr Pro Phe Val Val Leu Asn Ile Ser Val Asp Ser	
315 320 325	
gaa tgc gtt gat atc aat gtt act cca gat aaa agg caa att ttg cta	1059
Glu Cys Val Asp Ile Asn Val Thr Pro Asp Lys Arg Gln Ile Leu Leu	

980232_1.TXT

330	335	340	345	
caa gag gaa aag ctt ttg ttg gca gtt tta aag acc tct ttg ata gga				1107
Gln Glu Glu Lys Leu Leu Leu Ala Val Leu Lys Thr Ser Leu Ile Gly				
	350	355	360	
atg ttt gat agt gat gtc aac aag cta aat gtc agt cag cag cca ctg				1155
Met Phe Asp Ser Asp Val Asn Lys Leu Asn Val Ser Gln Gln Pro Leu				
	365	370	375	
ctg gat gtt gaa ggt aac tta ata aaa atg cat gca gcg gat ttg gaa				1203
Leu Asp Val Glu Gly Asn Leu Ile Lys Met His Ala Ala Asp Leu Glu				
	380	385	390	
aag ccc atg gta gaa aag cag gat caa tcc cct tca tta agg act gga				1251
Lys Pro Met Val Glu Lys Gln Asp Gln Ser Pro Ser Leu Arg Thr Gly				
	395	400	405	
gaa gaa aaa aaa gac gtg tcc att tcc aga ctg cga gag gcc ttt tct				1299
Glu Glu Lys Lys Asp Val Ser Ile Ser Arg Leu Arg Glu Ala Phe Ser				
	410	415	420	425
ctt cgt cac aca aca gag aac aag cct cac agc cca aag act cca gaa				1347
Leu Arg His Thr Thr Glu Asn Lys Pro His Ser Pro Lys Thr Pro Glu				
	430	435	440	
cca aga agg agc cct cta gga cag aaa agg ggt atg ctg tct tct agc				1395
Pro Arg Arg Ser Pro Leu Gly Gln Lys Arg Gly Met Leu Ser Ser Ser				
	445	450	455	
act tca ggt gcc atc tct gac aaa ggc gtc ctg aga cct cag aaa gag				1443
Thr Ser Gly Ala Ile Ser Asp Lys Gly Val Leu Arg Pro Gln Lys Glu				
	460	465	470	
gca gtg agt tcc agt cac gga ccc agt gac cct acg gac aga gcg gag				1491
Ala Val Ser Ser Ser His Gly Pro Ser Asp Pro Thr Asp Arg Ala Glu				
	475	480	485	
gtg gag aag gac tcg ggg cac ggc agc act tcc gtg gat tct gag ggg				1539
Val Glu Lys Asp Ser Gly His Gly Ser Thr Ser Val Asp Ser Glu Gly				
	490	495	500	505
ttc agc atc cca gac acg ggc agt cac tgc agc agc gag tat gcg gcc				1587
Phe Ser Ile Pro Asp Thr Gly Ser His Cys Ser Ser Glu Tyr Ala Ala				
	510	515	520	
agc tcc cca ggg gac agg ggc tcg cag gaa cat gtg gac tct cag gag				1635
Ser Ser Pro Gly Asp Arg Gly Ser Gln Glu His Val Asp Ser Gln Glu				
	525	530	535	
aaa gcg cct gaa act gac gac tct ttt tca gat gtg gac tgc cat tca				1683
Lys Ala Pro Glu Thr Asp Asp Ser Phe Ser Asp Val Asp Cys His Ser				
	540	545	550	
aac cag gaa gat acc gga tgt aaa ttt cga gtt ttg cct cag cca act				1731
Asn Gln Glu Asp Thr Gly Cys Lys Phe Arg Val Leu Pro Gln Pro Thr				
	555	560	565	
aat ctc gca acc cca aac aca aag cgt ttt aaa aaa gaa gaa att ctt				1779

980232_1.TXT

Asn	Leu	Ala	Thr	Pro	Asn	Thr	Lys	Arg	Phe	Lys	Lys	Glu	Glu	Ile	Leu	
570					575					580					585	
tcc	agt	tct	gac	att	tgt	caa	aag	tta	gta	aat	act	cag	gac	atg	tca	1827
Ser	Ser	Ser	Asp	Ile	Cys	Gln	Lys	Leu	Val	Asn	Thr	Gln	Asp	Met	Ser	
				590					595					600		
gcc	tct	cag	gtt	gat	gta	gct	gtg	aaa	att	aat	aag	aaa	gtt	gtg	ccc	1875
Ala	Ser	Gln	Val	Asp	Val	Ala	Val	Lys	Ile	Asn	Lys	Lys	Val	Val	Pro	
			605					610					615			
ctg	gac	ttt	tct	atg	agt	tct	tta	gct	aaa	cga	ata	aag	cag	tta	cat	1923
Leu	Asp	Phe	Ser	Met	Ser	Ser	Leu	Ala	Lys	Arg	Ile	Lys	Gln	Leu	His	
		620					625					630				
cat	gaa	gca	cag	caa	agt	gaa	ggg	gaa	cag	aat	tac	agg	aag	ttt	agg	1971
His	Glu	Ala	Gln	Gln	Ser	Glu	Gly	Glu	Gln	Asn	Tyr	Arg	Lys	Phe	Arg	
	635					640					645					
gca	aag	att	tgt	cct	gga	gaa	aat	caa	gca	gcc	gaa	gat	gaa	cta	aga	2019
Ala	Lys	Ile	Cys	Pro	Gly	Glu	Asn	Gln	Ala	Ala	Glu	Asp	Glu	Leu	Arg	
650					655					660					665	
aaa	gag	ata	agt	aaa	acg	atg	ttt	gca	gaa	atg	gaa	atc	att	ggg	cag	2067
Lys	Glu	Ile	Ser	Lys	Thr	Met	Phe	Ala	Glu	Met	Glu	Ile	Ile	Gly	Gln	
				670					675					680		
ttt	aac	ctg	gga	ttt	ata	ata	acc	aaa	ctg	aat	gag	gat	atc	ttc	ata	2115
Phe	Asn	Leu	Gly	Phe	Ile	Ile	Thr	Lys	Leu	Asn	Glu	Asp	Ile	Phe	Ile	
			685					690					695			
gtg	gac	cag	cat	gcc	acg	gac	gag	aag	tat	aac	ttc	gag	atg	ctg	cag	2163
Val	Asp	Gln	His	Ala	Thr	Asp	Glu	Lys	Tyr	Asn	Phe	Glu	Met	Leu	Gln	
			700				705					710				
cag	cac	acc	gtg	ctc	cag	ggg	cag	agg	ctc	ata	gca	cct	cag	act	ctc	2211
Gln	His	Thr	Val	Leu	Gln	Gly	Gln	Arg	Leu	Ile	Ala	Pro	Gln	Thr	Leu	
			715			720					725					
aac	tta	act	gct	gtt	aat	gaa	gct	gtt	ctg	ata	gaa	aat	ctg	gaa	ata	2259
Asn	Leu	Thr	Ala	Val	Asn	Glu	Ala	Val	Leu	Ile	Glu	Asn	Leu	Glu	Ile	
730					735					740					745	
ttt	aga	aag	aat	ggc	ttt	gat	ttt	gtt	atc	gat	gaa	aat	gct	cca	gtc	2307
Phe	Arg	Lys	Asn	Gly	Phe	Asp	Phe	Val	Ile	Asp	Glu	Asn	Ala	Pro	Val	
				750					755					760		
act	gaa	agg	gct	aaa	ctg	att	tcc	ttg	cca	act	agt	aaa	aac	tgg	acc	2355
Thr	Glu	Arg	Ala	Lys	Leu	Ile	Ser	Leu	Pro	Thr	Ser	Lys	Asn	Trp	Thr	
			765					770					775			
ttc	gga	ccc	cag	gac	gtc	gat	gaa	ctg	atc	ttc	atg	ctg	agc	gac	agc	2403
Phe	Gly	Pro	Gln	Asp	Val	Asp	Glu	Leu	Ile	Phe	Met	Leu	Ser	Asp	Ser	
			780				785					790				
cct	ggg	gtc	atg	tgc	cgg	cct	tcc	cga	gtc	aag	cag	atg	ttt	gcc	tcc	2451
Pro	Gly	Val	Met	Cys	Arg	Pro	Ser	Arg	Val	Lys	Gln	Met	Phe	Ala	Ser	
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980232_1.TXT

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 Arg Ala Cys Arg Lys Ser Val Met Ile Gly Thr Ala Leu Asn Thr Ser
 810 815 820 825

gag atg aag aaa ctg atc acc cac atg ggg gag atg gac cac ccc tgg 2547
 Glu Met Lys Lys Leu Ile Thr His Met Gly Glu Met Asp His Pro Trp
 830 835 840

aac tgt ccc cat gga agg cca acc atg aga cac atc gcc aac ctg ggt 2595
 Asn Cys Pro His Gly Arg Pro Thr Met Arg His Ile Ala Asn Leu Gly
 845 850 855

gtc att tct cag aac tgaccgtagt cactgtatgg aataattggt tttatcgag 2650
 Val Ile Ser Gln Asn
 860

atttttatgt tttgaaagac agagtcttca ctaacctttt ttgtttttaa atgaaacctg 2710
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 35 40 45
 Ala Gly Ala Thr Asn Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp
 50 55 60
 Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe
 65 70 75 80
 Glu Gly Leu Thr Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala
 85 90 95
 Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser
 100 105 110
 Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Ala Ser
 115 120 125
 Ala Lys Val Gly Thr Arg Leu Met Phe Asp His Asn Gly Lys Ile Ile
 130 135 140
 Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Thr Thr Val Ser Val Gln
 145 150 155 160
 Gln Leu Phe Ser Thr Leu Pro Val Arg His Lys Glu Phe Gln Arg Asn
 165 170 175
 Ile Lys Lys Glu Tyr Ala Lys Met Val Gln Val Leu His Ala Tyr Cys
 180 185 190
 Ile Ile Ser Ala Gly Ile Arg Val Ser Cys Thr Asn Gln Leu Gly Gln
 195 200 205
 Gly Lys Arg Gln Pro Val Val Cys Thr Gly Gly Ser Pro Ser Ile Lys
 210 215 220
 Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile
 225 230 235 240
 Pro Phe Val Gln Leu Pro Pro Ser Asp Ser Val Cys Glu Glu Tyr Gly
 245 250 255
 Leu Ser Cys Ser Asp Ala Leu His Asn Leu Phe Tyr Ile Ser Gly Phe

980232_1.TXT

			260					265				270				
Ile	Ser	Gln	Cys	Thr	His	Gly	Val	Gly	Arg	Ser	Ser	Thr	Asp	Arg	Gln	
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Phe	Phe	Phe	Ile	Asn	Arg	Arg	Pro	Cys	Asp	Pro	Ala	Lys	Val	Cys	Arg	
	290					295					300					
Leu	Val	Asn	Glu	Val	Tyr	His	Met	Tyr	Asn	Arg	His	Gln	Tyr	Pro	Phe	
305					310					315					320	
Val	Val	Leu	Asn	Ile	Ser	Val	Asp	Ser	Glu	Cys	Val	Asp	Ile	Asn	Val	
				325					330					335		
Thr	Pro	Asp	Lys	Arg	Gln	Ile	Leu	Leu	Gln	Glu	Glu	Lys	Leu	Leu	Leu	
			340					345					350			
Ala	Val	Leu	Lys	Thr	Ser	Leu	Ile	Gly	Met	Phe	Asp	Ser	Asp	Val	Asn	
		355					360					365				
Lys	Leu	Asn	Val	Ser	Gln	Gln	Pro	Leu	Leu	Asp	Val	Glu	Gly	Asn	Leu	
	370					375					380					
Ile	Lys	Met	His	Ala	Ala	Asp	Leu	Glu	Lys	Pro	Met	Val	Glu	Lys	Gln	
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Asp	Gln	Ser	Pro	Ser	Leu	Arg	Thr	Gly	Glu	Glu	Lys	Lys	Asp	Val	Ser	
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Ile	Ser	Arg	Leu	Arg	Glu	Ala	Phe	Ser	Leu	Arg	His	Thr	Thr	Glu	Asn	
			420					425					430			
Lys	Pro	His	Ser	Pro	Lys	Thr	Pro	Glu	Pro	Arg	Arg	Ser	Pro	Leu	Gly	
		435					440					445				
Gln	Lys	Arg	Gly	Met	Leu	Ser	Ser	Ser	Thr	Ser	Gly	Ala	Ile	Ser	Asp	
	450					455					460					
Lys	Gly	Val	Leu	Arg	Pro	Gln	Lys	Glu	Ala	Val	Ser	Ser	Ser	His	Gly	
465					470					475					480	
Pro	Ser	Asp	Pro	Thr	Asp	Arg	Ala	Glu	Val	Glu	Lys	Asp	Ser	Gly	His	
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Gly	Ser	Thr	Ser	Val	Asp	Ser	Glu	Gly	Phe	Ser	Ile	Pro	Asp	Thr	Gly	
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Ser	His	Cys	Ser	Ser	Glu	Tyr	Ala	Ala	Ser	Ser	Pro	Gly	Asp	Arg	Gly	
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Ser	Gln	Glu	His	Val	Asp	Ser	Gln	Glu	Lys	Ala	Pro	Glu	Thr	Asp	Asp	
	530					535					540					
Ser	Phe	Ser	Asp	Val	Asp	Cys	His	Ser	Asn	Gln	Glu	Asp	Thr	Gly	Cys	
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Lys	Phe	Arg	Val	Leu	Pro	Gln	Pro	Thr	Asn	Leu	Ala	Thr	Pro	Asn	Thr	
				565					570					575		
Lys	Arg	Phe	Lys	Lys	Glu	Glu	Ile	Leu	Ser	Ser	Ser	Asp	Ile	Cys	Gln	
			580					585					590			
Lys	Leu	Val	Asn	Thr	Gln	Asp	Met	Ser	Ala	Ser	Gln	Val	Asp	Val	Ala	
		595					600			</						

980232_1.TXT

Ala Val Leu Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp
740 745 750
Phe Val Ile Asp Glu Asn Ala Pro Val Thr Glu Arg Ala Lys Leu Ile
755 760 765
Ser Leu Pro Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Val Asp
770 775 780
Glu Leu Ile Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro
785 790 795 800
Ser Arg Val Lys Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val
805 810 815
Met Ile Gly Thr Ala Leu Asn Thr Ser Glu Met Lys Lys Leu Ile Thr
820 825 830
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Thr Met Arg His Ile Ala Asn Leu Gly Val Ile Ser Gln Asn
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980232_1.TXT

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